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TITLE: Compact, Integrated System for Processing Test Samples

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BACKGROUND OF THE INVENTION

Field of the invention

5 This invention relates to test devices and related instruments and systems that test biological, microbiological, chemical or other types of samples.

10 Description of related art

Biological and other types of samples can be reacted and subjected to chemical or optical analysis using various techniques, including transmittance and/or fluorescence optical analysis. The purpose of the analysis may be to identify an unknown biological agent or target in the sample, to determine the concentration of a substance in the sample, or determine whether the biological agent is susceptible to certain antibiotics, as well as the concentration of antibiotics that would be effective in treating an infection caused by the agent.

20 In the mid-to late 1970's, engineers and scientists working with the applicants' assignee and its predecessor in interest developed a technique for conducting optical analysis of biological samples using a sealed test sample card containing a plurality of small sample wells. The technique, and related instruments and devices, came to be known in the industry as the "Vitek ® System". The Vitek ® System was (and continues to be) a commercial success.

25 The cards used in the Vitek System are known in the patent literature, see e.g., U.S. Patents 4,118,280, 3,963,355, 4,018,65; 4,116,775 and 4,038,151. More recent versions of the cards are described in U.S. Patents Des. 382,647, Des. 414,272, 5,609,828, 5,746,980, 5,766,553, 5,843,380, 5,869,005, 5,916,812, 5,932,177, 5,951,952, and 6,045,758.

 Cards were developed for both identification of unknown microorganisms that may be present in a sample and susceptibility of a known organism to precisely calibrated concentrations

of antibiotics. During manufacture of the cards, the wells are filled with either various types of growth media for various biological agents, or else concentrations of different antibiotics, and covered with a transparent sealing tape.

The cards have an external transfer tube port as a mechanism for allowing a fluid sample 5 to enter the card. The cards further include an internal fluid passageway structure for allowing fluid to enter the wells of the card from the transfer tube port. One end of straw-like transfer tube is inserted into the transfer tube port. The other end is inserted into an open receptacle (e.g., test tube) containing the fluid sample to be tested. In accordance with the teaching of the prior art Charles et al. patent, U.S. Patent No. 4,188,280, the card with attached transfer tube and test 10 tube are placed into a stand-alone vacuum and filling sealing machine, known as the Vitek ® Filler Sealer. The filling and sealing machine generates a vacuum. When the vacuum is released, the fluid sample is drawn from the test tube into the transfer tube and through the internal channels of the card and into all of the sample wells. In the instrument of the prior art Charles et al. '280 patent, after the wells of the card are loaded with the sample, the cards are manually 15 inserted into a slot in a sealer module in the machine, where the transfer tube is cut and melted, sealing the interior of the card.

The cards are then manually removed from the filler/sealer module and loaded into a reading and incubating machine, known as the Vitek ® Reader, also described in the Charles et al. '280 patent. The reading and incubating machine incubates the cards at a desired 20 temperature. An optical reader is provided for conducting transmittance testing of the wells of the card. Basically, the cards are stacked in columns in the reading machine, and an optical system moves up and down the column of cards, pulling the cards into the transmittance optics one at a time, reading the cards, and placing the cards back in the column of cards.

The arrangement of the early Vitek System (as described in the Charles et al. '280 patent) has several limitations, in that two machines, a filler/sealer and a reader, are required to process and analyze the cards. Furthermore, additional time and labor are required to conduct the complete analysis of the card. The applicants' assignee later developed and commercialized a
5 fully automated instrument, referred to herein and known in the art as the "Vitek 2" instrument. The Vitek 2 instrument automates both the vacuum loading and sealing operations and combined them with incubation and reading in a single instrument. The overall instrument is described in several patents, including U.S. Patents 5,762,873 and 6,086,824, the contents of which are incorporated by reference herein.

10 Briefly, the "Vitek 2" system provides an automated sample testing machine that performs dilutions for susceptibility testing, fills the cards with the samples at a vacuum station, and seals the card by cutting the transfer tube, and conducts incubation and optical transmittance and fluorescence analysis of the cards, all automatically. The machine provides for novel pipetting and diluting stations, permitting fluids to be added to the test tubes or transferred from
15 one test tube to another. The machine is capable of conducting simultaneous susceptibility and identification testing of a sample placed in a single test tube. The machine provides for rapid, automatic identification and susceptibility testing of the sample.

The instrument uses a sample tray or "boat" and a test sample positioning or transportation system that moves the "boat" in four separate paths around a rectangular base pan
20 among the various stations. The user places a cassette loaded with cards and test tubes containing samples into the boat at a loading station. The design of the positioning system is such that it permits essentially a custom configuration of stations above the base pan. Expansion of the

machine to include additional carousels and reading stations, or addition types in intermediate procession stations such as dilution stations or vacuum stations, can be readily accomplished.

The test sample positioning system of the Vitek 2 instrument is described in U.S. Patents 5,736,102, 5,762,874, 5,798,182, 5,798,084, 5,853,667, and 5,897,835. The optical reading station is described in U.S. Patents 5,798,085, 5,853,666, and 5,888,455. The incubation station is described in U.S. Patents 5,925,884 and 6,156,565. The vacuum loading station is described in U.S. Patent 5,965,090. The cutting and sealing station is described in U.S. Patent 5,891,396. The entire content of all of the above-listed patents is incorporated by reference herein.

As was the case with the original Vitek System, the Vitek 2 system also has been a commercial success. The Vitek 2 system is particularly popular with larger clinics or testing laboratories that have a particular need for a high capacity and high throughput testing system. However, there are smaller labs and clinics that need that functionality and features of a state of the art diagnostic and sample-testing instrument, but do not necessarily require the high capacity and total automation as provided by the Vitek 2 system. There is a need in the art for a state of the art sample processing instrument, like the Vitek 2, but which is more compact, less-costly and less complex, and more suited to small and medium scale sample testing enterprises. The present invention provides an instrument and methods of operation that meets that need.

While this background discussion has set forth the context of the invention in relation to the closest known prior art, the various aspects and features of the inventive system are applicable to other types of sample testing and processing systems that are known in the art now or may later be developed. Thus, the inventors do not limit the scope of the invention to any particular sample testing device format, instrument or testing protocol. Moreover, the features of the present inventive system are applicable to other types of testing and other instrument

architectures besides biological sample testing and the particular instrument described in this specification. All questions concerning the scope of the invention are to be answered by reference to the appended claims.

SUMMARY OF THE INVENTION

In a first aspect, an integrated system for processing a plurality of test samples and test sample devices for receiving the test samples is described. The test samples are received in individual fluid receptacles. The instrument includes a carrier for carrying a plurality of the individual fluid receptacles and a plurality of the test sample devices. Each of the test sample devices are placed in fluid communication with a test sample stored in one of the individual fluid receptacles. The instrument further includes a vacuum station having a door so as to be adapted for manual insertion of the carrier into the vacuum station and manual removal of the carrier from the vacuum station. The vacuum station further includes a source of vacuum. The vacuum source is controlled so as to load the test samples from the individual fluid receptacles into the respective test sample devices.

The instrument further comprises a set of processing modules forming a carrier and test device processing subsystem. These modules are located remote from the vacuum station, i.e., the user must manually remove the carrier from the vacuum station and then manually load the carrier into the carrier and test device processing subsystem after completion of vacuum loading of the test samples. These modules include a module for conducting optical measurements of the test sample devices. The carrier and test device processing subsystem and the vacuum station are integrated into a single instrument.

In a second aspect, an integrated system for processing a plurality of test samples and test sample devices is provided. The system uses a carrier holding a plurality of the fluid receptacles and a plurality of the test sample devices in a spaced relationship, each of the test sample devices having a transfer tube providing fluid communication between the test sample device and one of the fluid receptacles received in the carrier. The system comprises a vacuum

station adapted for manual insertion of the carrier into the vacuum station and removal of the carrier from the vacuum station. A first door provides the user with access to the vacuum station. The instrument further includes a carrier and test device processing subsystem remote from the vacuum station. The carrier and test device processing subsystem includes modules or apparatus for sealing the test devices by cutting and sealing the transfer tubes, incubating the test devices, and reading the test devices. A second door is provided to give access whereby the user can manually insert the carrier to the carrier and test device processing subsystem.

In another aspect, a method is provided for processing a plurality of test samples contained in open receptacles with test sample devices. The receptacles and test sample devices are carried by a carrier. Each of the test sample devices have a transfer tube providing fluid communication between the test sample device and one of the fluid receptacles received in the carrier. The method comprises the steps of:

manually placing the carrier into a vacuum station having a chamber and applying vacuum to the vacuum station chamber to thereby transfer the test samples into the test sample devices as a batch;

manually removing the carrier from said vacuum station chamber after the transfer has been completed;

manually placing the carrier into an automated carrier and test device processing subsystem remote from the vacuum station, and

automatically moving the carrier with a transport system in the carrier and test device processing subsystem to modules automatically sealing the test sample devices and loading the test samples into an incubation station. The test devices are subsequently incubated and

periodically read by a reading station. The vacuum station and the carrier and test device processing subsystem are integrated into a single test sample processing instrument.

BRIEF DESCRIPTION OF THE DRAWINGS

Figure 1 is a perspective view of a preferred embodiment of a compact, integrated system for processing test samples and test sample devices. The instrument includes a vacuum station 5 on the left for vacuum loading of test sample devices that are received in a carrier, and a separate Carrier and Test Sample Device Processing Subsystem on the right which processes the carrier and test sample devices after the test sample devices are loaded by the vacuum station.

Figure 2 is a front elevational view of the instrument of Figure 1.

Figure 3 is a top view of the instrument of Figure 1.

10 Figure 3A is a front view of the instrument of Figure 1 with the front doors and panels open and the top panel and user access top removed.

Figure 3B is a detailed front view of the vacuum chamber with the door open showing placement of a loaded carrier with test sample devices and test tubes positioned within the vacuum chamber.

15 Figures 4 and 5 are diagrams of top and front views, respectively, of the instrument of Figure 1, showing the general location of specific sub-assemblies and sub-systems in the instrument; familiarity with these figures will be helpful in understanding the more detailed drawings in the subsequent figures, particularly Figures 16-21.

20 Figure 6 is an elevational view of a test sample device in the form of a multi-well test sample card. The instrument of Figures 1-5 is designed to process a batch of cards of Figure 6 at a time by means of a carrier. The carrier receives a plurality of the test sample cards of Figure 6 and a plurality of open receptacles, e.g., test tubes, containing a fluid sample to be tested.

Figure 7 is a perspective view of a carrier loaded with test sample devices and open receptacles. When the test sample devices and receptacles are placed in the carrier, each of the

test sample devices is placed in fluid communication with a sample in an open receptacle by means of a transfer tube, as shown.

Figure 8 is a perspective view of an empty carrier of Figure 7.

Figure 9 is another perspective view of an empty carrier of Figure 7.

5 Figure 10 is a top plan view of the carrier of Figure 7.

Figure 11 is a side elevational view of the carrier of Figure 7.

Figure 12 is a side elevational view of the carrier of Figure 7, opposite to that shown in Figure 11.

Figure 13 is an end view of the carrier of Figure 7, showing the handle.

10 Figure 14 is an opposite end view of the carrier of Figure 7.

Figure 15 is a bottom plan view of the carrier of Figure 7.

Figure 16 is a front perspective view of the instrument of Figure 1, with the waste collection and carrier loading/unloading doors removed, and with the front user access door removed.

15 Figure 17 is a perspective view of the instrument of Figures 1 and 16 with all of the instrument panels and doors removed, showing generally the front and left hand sides of the instrument, to better illustrate the subsystems and subcomponents of the instrument, in particular the vacuum, waste disposal, and test sample device reader subsystems.

Figure 18 is another perspective view of the instrument of Figures 1 and 16 with all of the 20 instrument panels and doors removed, showing generally the front and right hand side of the instrument, in order to better illustrate the subsystems and subcomponents of the instrument, in particular the waste disposal, sealer, and incubation station subsystems.

Figure 19 is a top plan view of the instrument of Figures 16 and 17.

- Figure 20 is a front elevational view of the instrument of Figures 16-19.
- Figure 21 is a perspective view of the top of the instrument with the top panel removed, in order to better illustrate the various components and subsystems of the instrument.
- 5 Figure 22 is a perspective, exploded view of the sealer station of Figure 20.
- Figure 23 is another perspective, exploded view of the sealer station of Figure 22.
- Figure 24 is an assembled, perspective view of the sealer assembly.
- Figure 25 is a side view of the card autoloader subassembly.
- Figure 26 is a perspective view of the card autoloader subassembly of Figure 25.
- Figures 27 and 28 are two perspective views showing the operation of the card autoloader
- 10 subassembly of Figures 25 and 26 loading cards into the incubation station of the instrument of
- Figure 1.
- Figure 29 is a perspective, exploded view of the transport assembly that moves the carrier of Figures 7-17 through the various modules or stations of the Carrier and Test Sample Device Processing Subsystem in the instrument of Figure 1.
- 15 Figure 30 is a top plan view of the transport assembly of Figure 29.
- Figure 31 is an end view of the transport assembly of Figures 29 and 30.
- Figure 32 is a detailed perspective view of the carrier-engaging block of Figure 29-31.
- Figure 33 is a view showing the movement of a loaded carrier past a detection station detecting the position of the carrier relative to a specific processing module in the instrument,
- 20 here the card autoloader subassembly of Figures 25 and 26.
- Figure 34 is a detailed flow chart showing the workflow and sequence of steps in the use of the instrument and associated carrier, test sample receptacles and test sample devices.

Figure 35 shows the incubation station with the front cover panel removed to better illustrate the carousel.

Figure 36 shows the incubation station with the carousel removed to show a slot in the air table that provides access for a thermometer to measure directly the air temperature in the

5 incubation station.

Figure 37 shows a portion of the front cover of the incubation station with a receptacle for receiving a thermometer.

Figure 38 is a side view of the portion of the incubation station of Figure 27 showing the receptacle holding the thermometer.

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DETAILED DESCRIPTION OF PREFERRED EMBODIMENT

5 **System Overview**

An overview of a presently preferred embodiment of a compact, high throughput instrument for processing test samples will now be described in conjunction with Figures 1-5. The details on the construction and operation of the instrument will be described later in
10 conjunction with Figures 6-34.

The instrument 10 processes a batch of test sample devices in the form of multi-well test sample cards in the illustrated embodiment. A representative test sample card 100 is shown in Figure 6 and will be described subsequently. The cards 100 are initially loaded in a cassette (carrier) 200 shown in Figures 7-15. The carrier 200 further carries a set of fluid receptacles (test tubes) 106 (Fig. 7) that contain a fluid sample. Each test sample device 100 is placed into fluid communication with an associated fluid receptacle 106 by means of a transfer tube 102, shown in Figures 6 and 7. The sample is loaded into the card by means of a vacuum loading station in the instrument 10 in the manner described below.
15

The instrument 10 of Figures 1-5 is a sample processing and data collection portion of an
20 overall sample testing system. The overall system includes a separate stand-alone identification station where bar codes on the test sample devices are scanned, the cards are loaded into the carrier 200, and the carrier is applied with a bar code and scanned. These functions are similar to the separate identification system described in the patent of Fanning et al., U.S. Patent 5,869,006, incorporated by reference herein. The overall system further includes a workstation having a
25 computer processing system that receives data from the reading system in the instrument. These

identification and computer processing aspects of the overall system are not particularly pertinent to the present invention and only insofar as they are relevant will they be discussed further.

The illustrated instrument was designed as a smaller and lower-cost alternative to more complex sample testing instruments, such as the system described in the above-referenced 5 Fanning et al. patent, for use in low to medium range applications in both the clinical and industry markets. The instrument provides for semi-automated filling, sealing, and loading of the test sample devices, as will be described in detail below. However, whereas the prior art Fanning et al. '006 patent and the Vitek 2 instrument supported automated diluting and pipetting 10 functions, these functions are performed off-line by the user either manually or using other equipment. In other words, the user prepares the samples so that they can be directly loaded into the test sample devices from their associated test tube. These off-line tasks will be discussed in more detail in conjunction with the work flow chart of Figure 34.

As in the case with the Vitek 2 instrument, the instrument 10 of Figure 1-5 provides a vacuum station 300 for inoculation of the fluid samples into the wells 104 of the test sample card 15 100 Figure 6. However, in the present system the vacuum loading is performed semi- automatically as described herein, not fully automatically. In particular, the user manually places the loaded carrier into the vacuum station. When the fluid samples enter the wells 104 of the card 100, the fluid sample rehydrates reagents previously loaded into the wells of the card at the time of manufacture.

20 After vacuum loading, the carrier 200 is then manually placed into a separate compartment in the instrument 10 containing a carrier and test sample device processing subsystem 50. This subsystem 50 includes a sealing station 400 which operates to seal the cards by cutting the fluid transfer tube 102. The instrument 10 includes a card autoloader sub-system

500 that automatically loads the cards 100 one at a time into an incubation station 600. The incubation station 600 includes a rotating carousel that holds the cards. The cards are held at a precisely controlled temperature. The incubation system includes a card eject mechanism that ejects the cards from the carousel one at a time and places the cards on a transport assembly 700
5 that carries the cards to a card reader subsystem 800. The card reader subsystem 800 includes transmittance optics stations that perform periodic colorimetric readings of the wells 104 of the cards 100. A software algorithm determines changes in patterns of individual reagent wells 104 and translates those patterns into organism identification or sets of antimicrobial results. When the reading is deemed complete, the cards 100 are sent by the card transport assembly 700 to a
10 card disposal system 900, which holds the cards for removal from the instrument by the user. If further reading is required, the cards are moved back into the incubation station 600 for further incubation and additional reading.

A carrier transport system 1000 is provided in the instrument for moving the loaded carrier 200 back and forth within the interior of the carrier and test sample device processing subsystem 50 of the instrument 10. The transport assembly 1000 is described in conjunction with Figures 29-33.
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The instrument of Figures 1-5 and 16-33 can be scaled up or down to offer capacity for processing 60 test sample cards at the same time, or even more. The present discussion will focus on an embodiment for sequentially processing six fully loaded carriers (60 test sample devices). It will be appreciated that by providing a larger carousel incubation station or a second
20 incubation station and second optics station and associated card transport assemblies the capacity could double.

The instrument 10 performs all control of sample well (test sample card) filling and incubation/optical reading. The instrument 10 also supports a two-step user workflow for test pre-processing: reagent hydration and sample inoculation (vacuum loading). The test pre-processing is followed by the steps performed automatically in the instrument: cassette and test setup verification using strategically placed bar code reader in the instrument, card transfer tube sealing, loading of test sample cards into the incubation station, reading of the cards, and unloading and return to the user of the processed carrier and test tubes. Upon loading of the cards 100 into the incubation system 600, the instrument controls incubation temperature, optical reading, and data transfer to the workstation computer processing system during the test processing period. The instrument then ejects the cards upon test finalization, by means of transport of the test sample cards into the card disposal system 900.

Door and User Interface Features (Figures 1-3B)

Referring primarily now to Figures 1-3B, the instrument 10 includes a set of panels 12 that cover the internal sample processing apparatus. The internal processing apparatus is described in more detail in Figures 16 et seq. The panels 12 include a hinged vacuum door 302 that provides access to a vacuum chamber 304, which are part of the vacuum loading system 300 in the instrument. The user places a fully or partially loaded cassette 200 (a set of up to 10 test sample cards 100, each connected to an associated test tube 106 via a transfer tube 102, as shown in Figure 7) into the vacuum chamber 304 in the manner shown in Figure 3B and closes the vacuum door 302. A vacuum is drawn in the chamber 304 and the release of vacuum loads the fluid samples into the wells of the test sample cards 100. As shown in Figure 4, the vacuum system 300 further includes a vacuum pump assembly 306 that supplies vacuum to the vacuum chamber 304.

The instrument further includes a hinged load/unload door 14. The user opens this door to expose a carrier loading and unloading station 16, best shown in Figure 3A, and introduces the carrier (loaded) into the carrier and test sample device processing subsystem 50. The loaded carrier 200 (with the vacuum loading just complete) is placed inside the machine at the carrier loading station 16 for subsequent processing in the instrument (sealing, incubation, reading, disposal). The transport system 1000 in the instrument engages the loaded carrier 200 and proceeds to move the carrier as a unit to stations in the instrument as described in detail below.

The instrument further includes a waste access door 902 which is part of the card disposal system 900. The door 902 is the means by which the user gains access to a waste compartment 904. A removable receptacle in the form of a bucket (906, Figure 16) is placed in the waste compartment 904. The test sample cards are dropped into the bucket 906 after the reading process is complete. When the bucket is full, the bucket is removed, the cards are discarded, and the bucket is replaced into the waste compartment 904.

The instrument further includes a front user access door 18, a top user access door 20, and top service panel side and rear panels, which are not relevant to the present discussion. These doors provide access for periodic cleaning of the instrument or service of components in the instrument. Access to the interior of the instrument 10 is restricted during processing for the safety of the user and to ensure uninterrupted processing of the cards. The instrument 10 monitors the status of all the doors via sensors. Doors that provide access to moving parts, such as the front user access door 18 and load/unload door 14, also have door locks that are monitored.

The vacuum door 302 and load/unload door 14 are round recessed doors. The doors pivot in opposite directions to provide an unobstructed transfer of the cassette 200 from the vacuum chamber 304 to the loading station 16. A detent in the hinge for these doors allows the door to stay open greater than 90° until the user is ready to close it. The hinges are recessed and hidden 5 from view when the doors are closed.

The instrument includes a compact user interface 22. The user interface includes a keypad and LCD screen, which are located on the user interface front panel, at the top left of the instrument 10 as shown in Figure 1. The instrument uses the screen to communicate messages about its operation and its status. An audible indicator is also used in conjunction with the LCD 10 display to notify the user when a task is complete or if an error has occurred. The keypad is used to respond to instructions, send commands to the instrument, and perform other functions. Indicator lights located next to the Vacuum Door and Load/Unload Doors provide additional status information to the user.

15

Test Sample Device 100 Features (Figure 6)

The illustrated embodiment is designed to process test sample devices in the form of multi-well test sample cards. Persons skilled in the art will appreciate that the instrument, and its 20 constituent components, can be configured to process other types of test sample apparatus, and the invention is not limited to any particular format or design for test sample apparatus.

A representative test sample card is shown in Figure 6. The card 100 is a flat, thin object having front and rear surfaces that are covered with a clear, oxygen permeable transparent sealing tape. The card contains 64 test sample wells 104 and an internal fluid passage network 25 108 that connects each of the wells to a fluid intake port 110 and fluid distribution manifold.

The fluid transfer tube 102 is automatically inserted in the fluid intake port 108 in the manner shown and locked in place using the teachings of O'Bear et al., U.S. Patent 6,309,890. During vacuum loading of the card, the fluid sample 120 enters the card 100 from the fluid transfer tube 102 and travels along the course of the internal fluid passage network 108. The fluid sample fills 5 the wells 104 of the cards, where the fluid rehydrates dried reagents or growth media. Under conditions of incubation, a reaction occurs between the reagents in the wells of the card and the microorganism in the fluid sample. As a result of this reaction, the transmittance of light though the wells changes. The optics in the instrument 10 periodically read the wells of the card 100 by obtaining transmittance measurements at particular wavelengths of light.

10 The cards for use with the illustrated embodiment are described at length in the patent literature and therefore a more detailed discussion is omitted. The reader is directed to the following U.S. Patents for further details: 5,609,828; 5,746,980; 5,670,375; 5,932,177; 5,916,812; 5,951,952; 6,309,890 and 5,804,437. Each of these patents is incorporated by reference herein.

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Carrier 200 Features (Figures 7-15)

Referring now to Figures 7-15, the carrier 200 or cassette is a molded plastic component 20 that holds a set of test sample cards 100 and associated test tubes 106. In the illustrated embodiment, the carrier 200 holds a maximum of 10 test cards in specially fitted slots 202. The front portion 204 of the cassette 200 has a test tube slot 206 for each test tube 106. The slots are numbered 1-10 across the front of the cassette for identification purposes. A handle 208 on the right side allows for one-handed carrying capability. A removable bar code label 210 is applied 25 to the opposite side of the carrier 200 in the flat panel portion 215 (See Figures 7 and 14). The

bar code 210 provides cassette identification when read by a bar code reader in the instrument

10. Each of the test sample cards is applied with a bar code 120, as shown in Figure 7.

The user loads the carrier 200 with tubes 106 of patient isolates (or, more generally, a fluid sample) and test cards 100 before placing the carrier in the vacuum chamber 304 (Figure 5 3A) for the filling process. The asymmetrical shape of the carrier 200 and receiving structures in the vacuum chamber 304 as shown in Figure 3B ensures that the carrier 200 is properly loaded into the instrument (i.e., the handle 208 is towards the front of the instrument). Upon completion of the vacuum loading process, the user opens the door 302 to the vacuum chamber 304 and removes the carrier 200 from the vacuum chamber 304 and places it in the load/unload station

10 16.

The carrier 200 is a main component of the transport system 1000. A special block feature in the transport system 1000 enables the transport system to move the carrier through the processing stations in the carrier and test sample device processing subsystem 50 and back to the load/unloading station 16. Optical interrupt sensors in the transport system detect slots 212 (Figures 8, 9 and 15) that are formed into the bottom of the carrier 200. The optical interrupt sensors and the slots allow the instrument microcontroller to track the cassette location. The interrupt slots 212 are U-shaped voids formed in a rib 214 formed in the bottom of the carrier 200. Each slot 212 is positioned in registry with the position of the card directly above it. Therefore, when the interrupt sensors detect the position of a slot 212, they are also detecting the 15 position of the associated card. This feature facilitates precise carrier positioning for automated sealing operations and automatic loading of the cards from the carrier 200 into the entrance slot 20 in the incubation station.

Vacuum Station 300 Features (Figures 1-4, 7, 17)

With reference to Figures 1-4 and 7, the user places a carrier 200 loaded with test sample cards 100 and test tubes 106, such as shown in Figure 7, into the vacuum chamber 304 of Figure 3A and closes the door 302. The vacuum process is activated via the user interface 22 keypad.

- 5 A silicon seal 306 on the vacuum chamber door 302 presses against the front panel surface 308, sealing the vacuum chamber 304. The vacuum pump in the vacuum pump assembly 306 (Figures 4, 17) starts drawing the air from the chamber 304. The air escapes from the card channels and wells via the transfer tubes and up through the suspension or fluid sample in the test tubes 106. The channels and wells inside of each card are now in a vacuum.
- 10 The vacuum station fills the card with the inoculation suspension in the test tubes 106 using vacuum displacement principles taught in Fanning et al., U.S. Patent 5,965,090, the content of which is incorporated by reference herein. The rate of change of the vacuum is monitored and regulated by a pneumatic servo feedback system under microcontroller control.

In particular, after a short period, the vacuum is released at a controlled rate from the 15 vacuum chamber. The increasing air pressure inside the chamber forces the suspension from each test tube 106 through the transfer tube 102 and into the internal fluid channels and wells 104 of the card 100. This process of course occurs simultaneously with all the cards in the carrier in the vacuum chamber. The result is vacuum loading of all cards 100 in the carrier 200. The carrier 200 is now ready for insertion into the loading station 16 of Figure 3A and 20 processing therein by the carrier and test device processing subsystem 50 in the remainder of the instrument 10.

Carrier and Test Sample Device Processing Subsystem (Figures 1, 4, 5, 16-33)

Now that the carrier 200 and test devices 100 have been processed in the vacuum station 300, the carrier 200 is now ready for placement into the loading station 16 and processed by the 5 remainder of the instrument's subsystems, collectively referred to herein as the carrier and test sample device processing subsystem 50. This group of components includes the transport system 1000, sealing station 400, card autoloader subassembly 500, incubation station 600, card transport subsystem 700, optical reading station 800 and disposal system 900. These features will be described in further detail in this section.

10

Carrier Loading and Unloading Station 16 (Figures 1, 3A, 16)

The load/unload station 16 is where the operator manually loads the carrier of filled cards to start the sealing, incubation, and reading processes. The load/unload door 14 (Figure 1) will remain locked at all times unless the user is ready to load or unload a carrier. The door 14 is 15 shown removed from the instrument in Figure 16 in order to better illustrate the loading/unloading station 16.

The loaded carrier 200 (Figures 3B, 7) is loaded into the instrument 10 through the open load/unload station door 14. A reflective sensor 1040 (Figure 17) in the load area is used to sense the presence of a carrier 200 in the load/unload station 16. An indicator light 32 above the 20 load/unload station 16 indicates the status of the load/unload station to the user. Once the door 14 is closed, the processing cycle automatically initiates.

The transport system 1000 (Figures 29 – 33) moves the carrier 200 by pulling or pushing it through each processing station within the instrument in the manner described below. The

instrument microcontroller keeps track of where the carrier 200 is located and the status of the transport system utilizing the slots 212 molded into the bottom of the carrier (described above) and optical sensors 1050 A-C (Figure 29) that are strategically placed in the transport system 1000. The transport system 1000 moves the carrier from the load/unload station 16 to a bar code scanner where the carrier bar code (Figure 7) and test sample bar codes are read, the sealer station 400, the card autoloader station 500 where the cards are loaded into the carousel incubation station 600, and back to the load/unload station 16 for removal of the carrier 200 and the test tubes plus transfer tube 102 remnants. The carrier is parked at the load/unload station 16, the door 14 unlocked and the operator notified by the load/unload indicator light 32. The carrier 200 can then be removed allowing disposal of the processed test tubes 106 and transfer tube 102 waste, making the carrier ready for testing of the next batch of test cards and associated fluid samples.

Bar Code Reader Station 60 (Figures 4, 5, 20, 17)

A bar code reader station 60 (Figures 4, 5) is positioned in the instrument 10 generally below the reading station 800. The station 60 automatically scans the bar code information on each carrier 200 and test card within the carrier 200 (see Figure 7) as they pass through the station. The bar code reader station 60 consists of a bar code scanner 62 (Figure 20) and a card sensor 1042 (Figure 17). The card sensor 1042 is located on the housing of the incubation assembly 600 as close to the cards in the cassette as possible. The card sensor 1042 confirms the presence of a card 100 in the carrier 200 and the slot location. The slots 212 in the bottom of the carrier allow the transport system 1000 to position each card in front of the bar code scanner 62.

As shown in Figure 7, each card 100 has a factory applied bar code 120 that includes information such as test type, lot number, expiration date and a unique sequence number. When the card bar codes 120 are scanned at the separate workstation at the time of loading cards into the carrier 200, the instrument's bar code reader 62 provides an additional level of security by verifying that the cards 100 are loaded as indicated by the user. If the bar codes are not scanned at the separate workstation ("load and go" mode), the lab technician's worksheet can be used for verifying that cards 100 are loaded in the carrier 200 as indicated.

Successfully scanned carriers 200 and test cards 100 are allowed to continue to the sealer station 400. Carriers 200 and cards 100 that cannot be read at the station 60 due to errors such as missing or damaged bar codes, expired cards, and unsupported card types, are returned to the load/unload station 16 and the user notified via the user interface 22 or indicator light 32. The user is given the opportunity to correct the problem and reload the carrier 200 within a limited amount of time.

15 Sealer Station 400 (Figures 4, 6, 7, and 17-24)

With reference to Figures 4, 6, 7, and 17-24, before a test card 100 can be incubated and read, the wells 104 of the test sample card must be sealed off from the outside environment. The sealer station 400 provides this function for all cards loaded into the carrier 200, one at a time. The sealer station 400 melts and seals the transfer tube 102 using a retractable heated nichrome wire 402, and thereby seals the cards. This operation will now be described in further detail.

After a carrier 200 is loaded into the instrument, a transport block in the transport system 1000 engages with the carrier 200 and pulls the cassette 200 along the transport system track through a carrier sensor 1040, a card sensor 1042, and the bar code scanner 62. If the carrier

passes inspection, it is moved back along the transport system 1000 track toward the load/unload door 14 where the sealer station 400 operates to cut and seal all the cards in the carrier 200.

In particular, as the carrier 200 moves through the station 400, the hot wire 402 is translated downwardly and at an angle through an aperture 404 in an enclosure or housing 406 to 5 the same elevation of the transfer tubes 102 in the carrier 200, and thereby exposed to each transfer tube 102. As the carrier 200 is slowly advanced by the carrier transport system 1000 each transfer tube is forced past the hot wire 402. The hot wire 402 causes the plastic transfer tube 102 to melt, separating the majority of the transfer tube, which falls into the test tube 106. The remainder of the transfer tube forms a short, sealed stub (e.g., 1.5 mm in length) extending 10 outward from the fluid intake port 110 in the card (Figure 6). At the completion of the sealing processing, power is cut off to the wire 402 and it is retracted back into its housing 406 to eliminate user contact. The temperature of the wire 402 is controlled by a microcontroller controlled constant current source, as described in Karl et al., U.S. Patent 5,891,396, which is incorporated by reference herein.

15 The overall operation of the sealer to cut the transfer tubes 102 is similar to the process described in the Karl et al. '396 patent. As cards 100 move past the sealer, the transfer tubes 102 are forced past the hot wire 402 melting the plastic and sealing the cards. The wire 402 and its associated assembly 408 then retracts into the housing 406. The carrier 200 is then moved to the card autoloader station 500, which moves the cards laterally off of the carrier 200 and into the 20 entrance aperture of the incubation system 600.

The sealer assembly 400 is unique in several respects: a) its method of electronic control, b) its mechanical alignment, c) a preloading feature where each card is biased against fixed

structures in the instrument prior to cutting and sealing the transfer tubes, and d) features preventing unauthorized user access.

As for feature a), a microcontroller ensures reliable cutting and sealing by maintaining a constant current in the hot wire 402 while retracting or extending the wire 400 through the 5 aperture 404 per the card/cassette cycle requirements.

As for feature b), the sealer housing or enclosure 406 orients a wire assembly 408 and associated drive mechanism 410 at an angle allowing alignment of the wire 402 using only one motor 412 to control the horizontal and vertical position. The wire alignment is achieved by adjusting the mounting of the housing 406 in the instrument or the alignment of the drive 10 mechanism 410 to the housing, and/or setting the limit positions of the motor 412 in firmware.

As for feature c) and d), the wire 402 and its associated assembly 408, and the drive mechanism 410 are ordinarily placed within the housing 406. A shield 416 covers the entrance aperture 406. When a card is in position for sealing, the motor 412 is energized and the motor 15 operates to move the wire assembly 408 down and at an angle through the aperture 406. This action causes the shield 416 to move out of the way to a retracted position. A spring-loaded pad 414 in the wire assembly 408 and located in front of the wire 402 makes contact with the edge of a card 100 and preloads or biases the cards 100 using a coil spring 415 against a fixed structure or stop in the instrument. The fixed structure is in the form of a rail 604 extending lengthwise along the face of the incubation station 600 housing 602. Other constructions are of course 20 possible. The wire 402 then cuts through the transfer tube to produce uniform stubs lengths as the cards 100 are moved past the stationary sealer wire 402. After the sealing operation is completed, the motor 412 is energized to retract the wire assembly 408 into the housing 406. As it does so, the rotating shield 416 retracts by gravity to a closed position covering the aperture

404. This covering of the aperture 404 prevents the user from gaining access to the retracted hot wire 402.

As the carrier 200 approaches the sealer station, the transport system 1000 slows its movement to a slow speed. The motor 412 in the sealer station 400 energizes to move the wire 5 subassembly 408 through the aperture 404 and expose the wire 402. The pad or "shoe" 414 is mounted approximately 2.0 mm in front of the sealer wire 402. The shoe is spring loaded by a compression spring 415 shown in Figure 22. The shoe or pad 414 mounts with a single shoulder screw 420 and incorporates an anti-rotation feature. As the card 100 approaches the hot wire 402, the shoe 414 makes initial contact with the card, deflecting the spring 415 and preloading 10 the card 100 against the rail 604 (Figure 27) on the incubation assembly panel 602. This insures consistency in transfer tube stub length. Forward motion of the carrier 200 past the hot wire 402 cuts the transfer tube 102, melting the plastic transfer tube 102 and sealing each card. After all 15 the cards 100 in the carrier are sealed, the transport system 100 again reverses direction along its track and each of the cards is placed in registry with the card autoloader system 500 for loading into carousel incubation station 600 to incubate.

The sealer wire 402 in the preferred embodiment is a heated 18 Gauge Chromel A wire mounted on a sliding block mechanism 422 inside the metal enclosure or housing 406. The 20 housing 406 positions the drive mechanism 410 at an angle, and locates the extended sealer wire/preload shoe 414 at the correct height, and prevents user access to the sealer wire 402 and drive mechanism. The drive mechanism 410 is mounted at an angle to simplify the horizontal and vertical alignment. A stepper motor 412 extends the hot wire mounting-block 426 at a 30° angle from horizontal to simultaneously adjust the horizontal and vertical position. This angle can of course vary in different embodiments and could vary for example between 20 and

70 degrees. The exact alignment of the sealer wire 402 is adjustable by firmware controlling the limits of the motor 412 to ensure a uniform stub length between 1.0 and 2.5 mm. When the cutting and sealing operation is finished, the stepper motor 412 retracts the hot wire assembly 408 until a flag 424 on the block 426 in the drive system is sensed by home position sensor 428 (see Fig. 22). The assembly includes a chain 448 that serves to protect a wire 446 supplying current to the cutting wire 402.

As the hot wire assembly 408 and mounting-block 426 is retracted, the rotating shield 416 drops down by gravity and covers the housing opening 404. The shield 416 has a tang 430 and flange 452. The flange 452 is positioned inside the elongate opening 454 in the housing 406 when the unit is assembled. The flange 452 contacts the shoulder 426 of the mounting-block 426 as the block 426 nears the retracted home position. The tang 430 and flange 452 prevents the user from lifting the shield 416 and gaining access to the hot wire. When the sealer motor 412 is energized, it causes the pin 462 to slide through the slot 460 in the drive mechanism 410 and thereby extends the hot wire mounting-block 422. The protective shield 406 is pushed open by the contact between the face of the block 422, which causes the shield to rotate upward, exposing the hot wire 402 and preload shoe 414. The microcontroller supplies a constant current to the wire 402 sufficient to produce the proper temperature for cutting through the transfer tubes as the cards pass by, melting the plastic and leaving a small stub of the tube to seal the interior of the card from the atmosphere.

20

Card Autoloader Station 500 (Figures 20 and 25-28)

Referring now to Figures 20 and 25-28, the instrument 10 further includes a card autoloader station 500 that loads sealed cards 100 into the incubation station 600. After the

cards have been sealed, the carrier 200 is moved to the autoloader station 500. The slots 212 in the bottom of the carrier 200 (Figure 8) allow the transport system 1000 to position each card directly in front of the incubator 600 entrance slot 610, shown best in Figure 28. The slot in the carrier is determined and tracked automatically by the instrument's internal microcontroller.

5 The autoloader station 500 includes a reciprocating, motor-driven pusher mechanism 502, located above the carrier 200. The mechanism 502 pushes the card 100 laterally off of the carrier 200 into the carousel (not shown) in the incubation station 600. The incubation station 600 carousel is a circular carousel oriented on its side (rotating about a horizontal axis) having 30 or 60 slots. One of the slots is positioned at the 6 o'clock position directly in alignment with the 10 card entrance slot 610. The pusher mechanism 502 returns home and the transport system 1000 and carousel index to the next card position. The loading of the next card in the carrier 200 proceeds in the same fashion. Upon completion of loading all the cards, the transport system 1000 returns the carrier 200 and test tubes 106 to the load/unload station 14 and notifies the user via the indicator 32 and user interface 22.

15 Referring now in particular to Figures 25-28, the autoloader includes a motor 504 that drives a block 506 attached to the card pusher mechanism 502. The block 506 has internal threads that engage a threaded shaft 510 extending laterally across the path of the carrier 200. As the motor 504 drives the block 506, the block 506 and attached pusher 502 slides along a guide 508. The pusher 502 contacts the cards 100 in the carrier and inserts them automatically into the 20 slot 610 in the incubation station 600. The tips 512 and 514 of the shaft 510 and guide 508 are received in apertures in a plate 612 mounted to the housing 602 of the incubation station as shown in Figures 27 and 28. A pair of guides 612 guide the cards 100 into the slot 610.

Incubation station 600 (Figures 16-20, 35-38)

The incubation station 600 in the instrument 10 will now be described in conjunction with Figures 16-20 and 35-38. The incubation station includes a circular carousel 604 (Figure 35). The carousel is covered by a set of removable access cover 630 forming an incubation enclosure. The carousel is rotated by means of a motor 632, shown in Figure 18. The structure and operation of the incubation station 600 and its associated carousel is basically the same as set forth in the patent literature, see U.S. Patents 6,024,921; 6,136,270 and 6,155,565, the contents of which are incorporated by reference herein. See also U.S. Patent 5,762,873. Accordingly, a detailed description of the construction of the incubation station 600 is omitted for the sake of brevity.

Once the test sample cards have been sealed and the cards loaded into the carousel via the entrance slot 610, they remain in the carousel 604 for the duration of the test period (up to 18 hours) or until the predetermined time allotment is met. The time allotment varies for each reagent or type of card. The carousel is contained in a temperature-controlled chamber (incubator), enclosed by the access cover 630.

The carousel 604 itself in a preferred embodiment is composed of four quadrants (called quadrocells or quads), as taught in U.S. Patent 6,136,270, together capable of holding up to 60 test cards within the incubator. Alternative configurations are possible. Positioning of the carousel is accomplished by optical sensors located at the top and bottom of the carousel, which read positioning slots on the outside edge of the carousel. Each carousel quadrant can be removed independently for cleaning. However, all four carousel quads must be in place in order for cards to be processed.

The incubator system regulates the temperature of the cards in the carousel. The

temperature is monitored and controlled through the use of precision thermistors monitored by a microcontroller maintaining at an average carousel temperature of $35.5 \pm 1^\circ\text{C}$. Access for a separate user installed probe thermometer has been provided to the front of the Incubator Cover, as explained below. This allows the user to verify the accuracy of the incubator temperature 5 using an independent calibrated thermometer. The rotating carousel system delivers test cards to the card transport system 700, which moves the cards to the reader station 800 four times an hour until the test is completed. The reader head optics scans each card and returns them to the incubator. The carousel includes a card eject mechanism 640 shown best in Figure 18 that 10 ejects a card from the 12 o'clock position in the carousel and places it in a test card transport system 700 (Figure 16) for transfer to the optics station 800 and return to the incubation station 600. This is the same as described in e.g., U.S. Patent 5,762,873.

FIG. 35 is a front perspective view of the carousel 604 and incubation station 600 of FIG. 1, with several of the cover panels of the incubation station removed in order to better illustrate the carousel 604. The cover panels form an enclosure for the carousel 604 and isolate the 15 carousel 604 from ambient conditions.

The carousel 604 is vertically mounted and rotates about a horizontal axis. An air duct 622 is provided on the upper portion of the station 600 to allow air to circulate from the front portion of the incubation station (containing the carousel 604) to the rear of the station behind the bulkhead 652. A small hole is placed in the rear cover panel parallel to and positioned behind the 20 bulkhead 652 to allow a controlled amount of ambient air into the station. The duct 622 includes an aperture in the bulkhead 652 to allow air to flow down the rear side of the bulkhead between the bulkhead and the rear cover panel, where it is blown over a heater which heats the air, and

blown by a second fan into an air distribution table 624 positioned behind the carousel 604, in the manner shown in Figure 36.

The carousel 604 has a plurality of slots 614 for receiving the test sample cards. The carousel has a substantially open front side portion 623 through which the cards are introduced 5 into the slots 614 at the lowermost portion of the carousel at the carousel loading station, and an opposite rear side portion facing the air table 624 and the bulkhead 652.

FIG. 36 is a perspective view of the incubation station of FIG. 35 with the carousel 604 removed, in order to better illustrate the air table 624 and air distribution cover plate 625 features of the incubation station. The air table 624 receives warm air from a heater and fan assembly 10 behind the bulkhead 652. The air table 624 has an air distribution cover plate 625 that encloses the air table 624 which is positioned in registry with the slots 614 of the carousel 604. The cover plate 625 has a plurality of elongate openings 626 formed therein that direct the warmed air over the rear side portion of the carousel and over the cards in the carousel slots. In order to promote adequate air flow over the cards, the rear side portion of the carousel adjacent to and opposite the 15 air distribution cover plate 625 is substantially open and free of obstructions so as to permit substantially uninterrupted air flow over the test sample cards.

A notch 670 is formed adjacent to the side of the air table to allow access for a thermometer probe to the interior of the air table 624 to thereby allow a user to obtain an instantaneous temperature reading of the air in the air table, prior to the air flowing over the test 20 sample cards. As shown in Figure 37, an insert retainer or receptacle 672 is mounted to the cover panel 602 of the incubation station housing in registry with the notch 670 to thereby provide a means for holding the thermometer in place. The receptacle 672 includes a tang 674 which grips the thermometer 676, as shown in Figure 38. The face of the thermometer 676

includes a display for displaying the temperature. The thermometer 676 probe is shown in dashed lines in Figure 38.

The temperature monitoring system described herein is believed unique in its application to a instruments of this type. The present design simplifies the integration of a direct readout 5 thermometer 676. The thermometer is able to measure the incubator air table temperature using the retainer 672 to position the thermometer tip at the appropriate angle and location inside the air table 624. The external thermometer 676 gives a direct and accurate reading of the internal temperature without disturbing the ongoing test.

Our temperature monitoring system has many unique features, the most significant of 10 which is the location of the external thermometer. The thermometer probe is positioned in such a way that it monitors the warm air directly before the air hits the cards. This location is significant because the air cools slightly as it crosses the cards, and the temperature to monitor is the air temperature as it begins to hit the cards. Extensive testing was performed to find an accessible location that accurately reflects the internal temperature of the incubator. The 15 positioning of the thermometer is important and is aided by several unique features of the system. First, there is the notch 670 molded into the incubator chassis where the tip of the thermometer probe fits (see Fig. 36). This notch allows the thermometer to measure the air flowing behind the air table, which would otherwise be unreachable. The second unique feature of the thermometer positioning is the thermometer retainer or receptacle 672, as seen in Figure 20 38. This mount holds the thermometer 676 at an angle necessary to position the probe in the notch (see Fig. 38). The angled entrance allows the probe to pass over the carousel without interfering with the carousel motion. It also holds the thermometer at the appropriate distance from the front of the incubator bulkhead 652 so the tip of the probe does not hit the bulkhead.

The mount also has a clip 674 to hold the thermometer in place. The thermometer is snapped into the receptacle 672 and is not able to slide along any of the three axes that would affect its visual reading. The thermometer can rotate in place, though, as this does not affect the accuracy of the temperature readings.

5 A convenient point for the user is that the system was designed to use a standard traceable 1/8 in diameter probe thermometer. Should the thermometer break or lose calibration, it can be easily replaced. The snap-in receptacle also allows the thermometer to be easily removed for cleaning and calibration. Though this external monitoring system was designed with the industry users in mind, clinical users also appreciate the ease of manually verifying the 10 temperatures reported by the instrument firmware. Another benefit is that the temperature reported by the thermometer is instantaneous. The firmware only reports incubator temperature as a running three-minute average. Should the instantaneous temperature be needed, the user can easily measure it manually. Suitable thermometers 676 include Fisher Scientific Traceable Jumbo Display Digital Thermometer (part no. 14-648-47) and VWR Scientific Products Jumbo 15 Display Digital Thermometer (part no. 77776-720).

Card Transport System 700 (Figure 16, 17 and 20)

As best shown in Figures 16, 17 and 20, the instrument includes a card transport system 20 700 that transfers the cards from the incubation station 600 past the optical reading station 800 for reading of the wells 104 in the cards 100. The card transport system 700 is essentially the same as described in the prior U.S. patents 5,798,085; 5,853,666; and 5,888,455, which are incorporated by reference herein. Accordingly, a more detailed description is omitted for the sake of brevity. Basically, the card is held in a vertical attitude between a belt 704 and a ledge

702 and moved from right to left and left to right by means of a motor driving the belt 704 back and forth. The ledge includes a slot feature for holding cards in the vertical position as the belt drives the cards back and forth. As the cards are moved past the transmittance optics heads, the cards are moved in a precise fashion as explained below to obtain transmittance measurements 5 for each of the wells in the card at a multitude of positions across the width of the wells. The card includes built-in alignment sensor stop holes 130 (Figure 6) to accurately position the wells in the optical system.

Reading Station 800 (Figures 4, 5, 16 and 17)

10 Once the cards are placed in the card transport system 700, they are moved past the reading station 800. The reading station includes two transmittance optics modules 802 (see Figures 16 and 17) that are oriented vertically, in the same direction as the columns of wells in the card. Each module 802 obtains measurements from one column of wells. Together, the modules 802 obtain transmittance measurements of the wells of the card in two columns of wells 15 at the same time. The construction and manner of operation of the optical reader station 800 is essentially the same as described in the prior U.S. patents 5,798,085; 5,853,666; and 5,888,455, therefore only a general overview and discussion will be set forth herein for sake of brevity. Unlike these patents, the illustrated embodiment provides only transmittance measurements, but 20 of course fluorescence measurements could be taken as described in these patents by either replacing one of the modules 802 with a fluorescence module (see U.S. Patent 5,925,884) or adding a fluorescence module to provide three modules. Additional modules of course could be provided.

The card 100 is positioned and read by the transmittance optical system modules 802 and

returned to the carousel slot from which it was ejected. No data analysis takes place in the instrument; optical data is collected and transmitted to a remote workstation for analysis. Raw data may be queued and transmitted to the workstation later, in the event that communications between the instrument and workstation is not occurring.

5 The reader station 800 scans each of the cards 100 once every fifteen minutes, for four scans per hour. Each time the card is read, it returns to the carousel to be incubated until the next reading cycle. After the last reading cycle is complete, the card is transported through the optics to the card disposal system 900 for card ejection into the waste collection container.

The reader system 800 and card transport system 700 together performs card positioning
10 and optical data collection in order to periodically monitor the growth of organisms inside the wells of the test cards. Optical transmittance data is used to quantify organism growth by measuring the optical transmittance of each well versus time. The illustrated embodiment currently supports two types of optics modules 802. The first module 802 has 660nm LEDs
15 illumination sources for each well. The other module 802 has 428nm and 568nm LEDs for each well. Development of a third module with additional wavelengths is of course possible.

Each optics module 802 has 8 measurement LEDs so that it can read 8 sample wells per column. Each card has 8 (or 16) columns of wells for a total of 64 wells per card. Each module 802 includes not only the transmittance LED light source for each well but also a detector for each well that captures the LED light after passing through the well. The detectors use silicon photodiodes. Sampling takes place as the card, with its 8 columns of 8 sample wells, moves through the optical path (from LED to photodiode) of the modules 802. The reading system 20 scans across each well as the card is moved by the transport system 700 in 16 spatially separated steps, taking 3 readings per step. This data is then processed to reduce the effect of any bubbles

that may have formed in the wells. The readings are smoothed and the peak value is chosen.

The emitter and detector housings in the modules 802 are hinged for ease of servicing and access to the optics area for cleaning. This detection system is capable of auto calibrating internally through air for 30% to 100% transmission (no light to full light). The optics is calibrated to 100% transmission through air automatically before reading each card.

5

Disposal System 900 (Figures 16, 17, 20)

Once incubation and optical testing of a test sample card 100 is complete, the card is automatically removed from the carousel in the incubation station 600, passed through the reader 10 station 800, and transferred to a disposal system 900. The disposal system includes a disposal enclosure 904 that holds a waste container 906, and a ramp 908 that directs the card from the edge of the card transport system 700 into a chute 910 positioned directly above the waste container 906. The waste container is removable from the instrument 10 and is accessed via the door 902 shown in Figure 1. The card is transported to the ramp 908 simply by operating the 15 belt in the transport system 700 to the left to carry the card past the edge of the left-hand ledge 702.

The waste collection station 900 is located below the vacuum station 300 at the front of the instrument 10. It houses a removable waste container 906 (see Figure 16) and a sensor (not shown) to detect when the container is installed. The user is notified when the waste container 20 906 is full or jammed by means of the user interface 22. Software in the instrument tracks the number of cards added to the container after it has been emptied.

Carrier Transport system 1000 (Figures 29-33)

The instrument 10 includes a system 1000 for transporting the carrier 200 from the loading and unloading station 16 through the carrier and test device processing subsystem 50. The transport system 1000 is shown isolated in Figures 29-33 in order to better illustrate the components of the system. Their interrelationship with the various modules in the instrument 10 will be appreciated from inspection of the remaining figures, e.g., Figures 17, 19 and 20, and from the following discussion.

Basically, the transport system 100 includes the carrier 200 and a transport subassembly 1002 that moves the carrier 200 back and forth. The transport subassembly 1002 includes a cassette-engaging member 1004 in the form of a block that is adapted to engage the carrier in the manner described below. The transport subassembly 1002 is constructed and arranged such that it moves the block 1004 and the carrier 200 back and forth along a single longitudinal axis between the carrier loading and unloading station 16, the sealing station 400, and the incubation loading station 500.

The transport subassembly 1002 includes a linear actuator motor 1006 that rotates a threaded shaft 1010. The threaded shaft 1010 is received in a threaded nut 1005 (Figure 32) that is attached to the block 1004. A cylindrical guide member 1008 extends between a motor/guide rod mount 1018 and a front bearing mount 1020. The front bearing mount 1020 is fastened to the base 1016 of the transport subassembly 1002 as shown in Figure 29. A pair of lift pins 1012 extend upwards from a drive nut engagement slide 1022 through apertures 1024 in the block 1004. The lift pins are biased by springs 1026 to a lower position, such that when the block 1004 is positioned at the loading/unloading station 14, the lower edge of the lift pins 1012 are in contact with a ramp or cam surface 1014 formed in the base 1016. When the block 1004 is

5 moved by the motor 1006 towards the rear of the instrument, the lift pins ride up the ramp 1014 and thereby extend through the apertures 1024. In this upper position, the lift pins can then make contact with features on the underneath side of the carrier 200 and thereby pull the carrier along the track 1030 as the motor 1006 moves the block 1004 towards the rear of the instrument to the bar code reading station 60.

In operation, a reflective sensor 1040 positioned on the side of the incubation station housing as shown in Figure 17 detects the presence of a carrier in the loading and unloading station 16. As the linear actuator motor 1006 rotates the shaft 1010, the block 1004 is moved from the front of the instrument 10 and the two lift pins 1012 are lifted to engage the test sample 10 carrier 200. The pins 1012 are lifted by means of the cam surface 1014 molded into the base 1016 of the transport subassembly 1002. The pins 1012 are attached to the drive nut engagement slide 1022, which holds ball bearing wheels (not shown). The ball bearings ride up the cam surface 1014, lifting the pins 1012, when the motor 1006 is indexed to move the block 1004 to the rear of the instrument. The carrier 200 is then dragged into the instrument past a second 15 reflective sensor 1042 (also shown in Figure 17), which counts the number of test sample cards and determines their location in the carrier. The carrier 200 and its test sample cards are then presented to the bar code reader station 60, which reads the bar codes on the test sample cards 100 and the carrier 200.

After the bar codes are read, the motor reverses and moves the carrier toward the front of 20 the instrument towards the loading and unloading station 14. During the forward travel the hot wire in the sealing station 400 is deployed and the test sample cards are sealed. The motor 1006 reverses again and the carrier 200 is moved to the card autoloader station 500 and placed into

position where the test sample cards can be pushed off the carrier 200 and into the incubation station 600.

Three optical interrupt sensors 1050A, 1050B and 1050C (Figures 29 and 30) track the position of the carrier 200 over the entire travel. The three sensors 1050 are mounted to a single printed circuit board 1052 that is snapped into the transport subassembly base 1016. The carrier 5 200 slides over removable and replaceable wear strips 1054. The wear strips 1054 minimize friction between the carrier 200 and the base 1016.

As noted above, the linear actuator stepper motor 1006 moves the block 1004. The block 1004 restrains the lift pins 1012. The motor's shaft 1010 extends nearly the entire length of the 10 1002. The end of the shaft 1010 rotates in a pillow block bearing 1020 shown best in Figure 29. The motor end mounts into an aluminum bracket 1018. The motor 1006 is 15 mounted to the bracket 1018 indirectly via four vibration control grommets and shoulder screws.

The rotating motor 1006 drives an acme threaded nut 1005 (Figure 32) along the length of the shaft 1010. The nut 1005 is pressed into the aluminum block 1056, which is coupled 15 indirectly to the drive block 1004 via two vibration control grommets 1058 and shoulder screws 1060. The shoulder screws 1060 allow the nut 1005 to self align, preventing the nut 1005 from binding with the shaft 1010. The grommets 1058 prevent noise generated by the nut 1005 from transmitting through the drive block 1004 and into the base 1016.

The drive block 1004 is moved horizontally by the nut 1005. When moving toward the 20 front of the instrument, a bearing surface 1060 on the block 1004 pushes the rear surface 220 (Figure 14) of the carrier 200. When moving toward the back of the instrument, the two lift pins 112 lift through the holes 1024 in the drive block to engage a rib 222 on the underside of the sample carrier (see Figure 15).

When the drive block 1004 is at the front, the block functions as a stop for a new sample carrier 200 being inserted into the instrument. When the drive block 1004 is at the back of the instrument, a reflective sensor 1064 (Figure 29) detects it and indicates to the instrument microcontroller that the block 1004 is in its home position.

5 Three optical interrupt sensors 1050A, 1050B and 1050C are mounted to the printed circuit board 1052. The use of the circuit board 1052 eliminates the wires screws required when mounting the sensors directly to the base 1016. The sensors 1050A, 1050B and 1050C detect the notches 212 on the underside of the carrier 200, as explained above. Each notch corresponds to the location of a test sample card. The sensors are located on the printed circuit board at the card 10 counter reflective sensor position (sensor 1050A), the bar code reading position (sensor 1050B), and the incubator loading position (sensor 1050C). The sensors 1050 A-C allow the carrier's 15 position to be continuously monitored.

The lift pin subassembly consists of two vertical pins 1012 mounted into an aluminum block 1022 containing two ball bearing rollers (not shown) at the base of the pins, functioning as wheels. The horizontal surface 1066 the wheels roll on is stepped near the front of the instrument to provide the cam or ramp surface 1014. The step is angled to allow the wheels to roll up and down, raising and lowering the pins 1012. Compression springs 1070 on the pins 15 between the drive block 1004 and the body of the lift pin subassembly ensure that lift pin subassembly drops when rolling down the cam 1014.

20 Rails 1072 are provided to constrain the carrier's motion to forward and backward. The wear strips 1054 are mounted on the left and right horizontal surfaces of the base 1016 as shown in Figure 29 to provide a low friction and wear surface for the carrier 200 to slide on.

The front cover 602 of instrument incubator station 600 provides three functions for the transport system. Firstly, a horizontal rib 1080 (Figure 17) prevents test sample cards from sliding off the right side of the carrier 200 prior to insertion into the incubation station 600. Secondly, the reflective sensor 1040 (also Figure 17) mounted near the front determines when 5 the carrier 200 is present in the loading station. Thirdly, the sensor 1042 mounted just behind the sensor 1040 counts the test sample cards 100 and determines their location on the carrier 200.

As best shown in Figures 3A and 16, the front panel of the instrument has a tapered entryway in the loading and unloading station 16 for loading for the carrier 200. The carrier 200 is inserted until it contacts the drive block 1014. The door 14 is closed and the sensor 1040 10 registers the carrier's presence. The space between the door 14 and drive block 1004 is such that the reflective sensor 1040 will always detect the carrier 200 if it is present in the loading and unloading station.

Control Electronics and Firmware

15 The instrument 10 includes control electronics and firmware for controlling the operation of the various modules and subsystems of the instrument. The control electronics is conventional. Such electronics and firmware can be developed with ordinary effort by persons skilled in the art from the present disclosure, given the present state of the art.

20

Work Flow (Figure 34)

The work flow and processing steps for the instrument 10 will now be described in conjunction with Figure 34 together with the other Figures. At step 1100, the user prepares the 25 sample inoculum off line, loads the fluid samples into the test tubes, scans the bar codes on the cards 100, and loads the cards 100 and test tubes into the carrier (cassette) 200. The bar code

may be scanned off line with a separate bar code scanner. The scanning steps may be performed at a separate identification station having a workstation or computer programmed to receive information regarding the samples being tested, the scans of the bar codes on the cards being used, and the scan of the carrier bar code.

5 At step 1102, the user opens the vacuum chamber door 302 and loads the loaded carrier (as in Figure 7) into the vacuum chamber 304, see Figure 3A. The user then closes the door 302 to thereby seal the chamber.

At step 1104, the user initiates the vacuum cycle filling the cards via the user interface 22 keypad.

10 At step 1106, the vacuum pump is energized and a vacuum is generated inside the vacuum chamber 304. The vacuum displacement fills the cards in the carrier in the manner described above.

At step 1108, a test is made to see if the reagent fill was successful. The vacuum slope and time are monitored to insure reagent fill.

15 At step 1110, if the reagent fill was not successful, the carrier processing is aborted as indicated at step 1112 and the user removes the carrier 200 the vacuum station 300.

At step 1114, if the reagent fill was successful, the user unloads the carrier 200 from the vacuum chamber 304.

At step 1116, the user opens the door 14 and manually places the carrier into the loading and unloading station 16. The detection of the carrier is made by the sensor 1040 (Figure 17).

20 At step 1118, the transport system 1000 moves the carrier 200 to the bar code reader station 60. En route, the cards 1000 loaded into the carrier are detected by the card sensor 1042 (Figure 17).

At step 1120, the bar codes in the carrier and on the cards are read by the bar code scanner in the reader station 60. The bar codes for the carrier and the cards are compared to the bar codes scanned off-line (if such scanning was done).

At step 1122, the instrument determines whether the bar code read was successful. If not, 5 the process proceeds to step 1124 where the transport system 1000 moves the carrier back to the loading/unloading station 16 and the door 14 is unlocked. At step 1126, the user corrects errors if possible.

If the bar code read was successful, the process proceeds to step 1128. At this step, the transport system moves the carrier to the sealer station 400.

10 At step 1130, the sealer station 400 operates to seal each of the test sample cards in the carrier in the manner described above. The transfer tube remnants fall into the test tubes. The remaining stub seals the test sample cards.

At step 1132, a check is made to determine whether the seal of all the cards was successful. This is done by monitoring the hot sealer wire current, monitoring the sealer motor 15 steps, and monitor the transport motor steps, and if there are no errors, the sealer worked.

If the sealing step was not successful, the process proceeds to step 1142 and the test is aborted and the processing proceeds to step 1138.

If the sealing step was successful, the transport system 1000 moves the carrier 200 to the card autoloader system 500, as indicated at step 1134. The card autoloader is described 20 previously.

At step 1136, the card autoloader station 500 operates to load the cards one at a time into the carousel in the incubation station 600. The incubator carousel may rotate or index to any available position to accommodate the next card.

At step 1138, after step 1136 is completed, the transport system 1000 moves the carrier 200 with the test tubes and transfer tube remnants to the loading and unloading station 16.

At step 1140, the user removes the carrier 200 and disposes of the test tubes and their contents. The carrier is now ready for reuse.

5 At step 1144, the cards 100 are now housed in the incubation station 600 where they are incubated at a constant temperature.

At step 1146, the cards are periodically pushed out of their slot in the carousel and placed into the card transport system 700, where they are shuttled back and forth to the reading system 800. The reading of all the wells in the card is designed to occur at every 15 minutes.

10 At step 1148, the transmittance measurements obtained by the optics modules 802 are transmitted to the separate workstation via communications ports or interfaces in the instrument 10.

15 At step 1150, a check is made to determine if the reading of the cards is complete. This would occur such as by whether a reaction has occurred in one or more of the wells such that the periodic reading of the cards indicates that identification of the sample or susceptibility of the sample can be determined. If the test is not complete (i.e., more reading needs to occur), the processing proceeds to path 1152 and the card is sent back to its slot in the carousel for more incubation and additional reading, and steps 1144, 1146, 1148 and 1150 repeat.

If, at step 1150, the reading is complete, a check is made to see if the waste container in 20 the disposal station enclosure 904 is full. If so, the user is notified at step 1158. If not, the card transport system 700 moves the card all the way to the left past the end of the ledge 702 and the card falls into the disposal system chute 910 and lands in the waste container in the enclosure 904.

At step 1162, the user periodically empties the waste container.

From the foregoing description, it will be appreciated that we have described a method for processing a plurality of test samples contained in open receptacles 106 with test sample devices 100, the receptacles and test sample devices carried by a carrier 200; each of the test sample devices 100 having a transfer tube 102 providing fluid communication between the test sample device 100 and one of the fluid receptacles 106 received in the carrier 200, as shown in Figure 7. The method comprises the steps of:

manually placing the carrier 200 into a vacuum station 300 having a chamber 304 and

applying vacuum to the vacuum station chamber 304 to thereby transfer the test samples into the

test sample devices 100 as a batch;

manually removing the carrier 200 from the vacuum station chamber 304 after the

transfer has been completed;

manually placing the carrier 200 into an automated carrier and test device processing

subsystem 50 remote from the vacuum station 300, and

automatically moving the carrier with a transport system 1000. The carrier is moved in a

test device processing subsystem 50 which has modules that automatically a) seal the test sample

devices (sealer station 400), b) incubate the test sample devices (incubation station 600), and c)

read the test sample devices (reading station 800). As shown in the Figures, the vacuum station

300 and the carrier and test device processing subsystem 50 are integrated into a single, unitary,

compact test sample processing instrument 10.

Variation from the specifics of the disclosed embodiments are to be expected depending on the configuration of the test devices and other factors. The scope of the invention is to be determined by reference to the appended claims, in view of the above.